Q & A

Carles Lalueza-Fox

Carles Lalueza-Fox is a researcher at the Institute of Evolutionary Biology (CSIC-UPF) in Barcelona, where he directs a small group that focuses on paleogenomics. He obtained his Ph.D. in Biology at the University of Barcelona in 1995, and spent one year in Cambridge and another one in Oxford as a postdoc. He has published many papers on paleogenetics of extinct animals, past human populations and archaic hominins. In recent years he has been mainly working on Neanderthals, collaborating with Svante Pääbo in the Neanderthal Genome Project. Besides his research, he is interested in communicating science to the wider public and has published seven popular books on human evolution, human diversity and paleogenetics, for which he has won several prizes. He loves mountaineering and, besides numerous routes in the Pyrenees and the Alps, he has ascended the Kilimanjaro and the Aconcagua, the highest mountains in Africa and the Americas, respectively.

How did you get into biology? My father used to buy many books on history, archaeology and evolution, which unfortunately he never had time to read — but I did! I specially remember F. Clark Howell's "Early Man" (1969) and C.W. Ceram's "Gods, Tombs and Scholars" (1949), because both managed to portray the search for our past as a romantic adventure. I was fascinated by all things related to the discovery of the past and started a huge collection of invertebrate fossils (mainly trilobites) and also one of Roman imperial denarii coins, which I am still pursuing. After the unavoidable boredom at school, during which I dedicated my attention to drawing and painting — my only natural talent — I decided to study biology. I (re)discovered anthropology and the fascination of human fossils, and, thanks to the PCR technique, of directly retrieving genes from these past remains. I did the first PhD on ancient DNA in Spain, but it was only later, during my postdoc at Oxford with Alan Cooper and the late Ryk Ward, that I came to live science with a passion.

Those were the ancient days of ancient DNA weren't they? Yes, and I am old enough to have lived through all the crucial developments on the field — including the bizarre claims of dinosaur DNA retrieval, the seemingly unsolvable problems of contamination and the recent revolution of next-generation sequencing technologies. Things are very different now — the ancient DNA groups are no longer composed of experimentalists but of bioinformaticians. Nevertheless, without any doubt we are now at a truly fascinating moment in this field and I feel privileged to take part in it.

What was your favourite ancient DNA moment? Without a doubt, the first retrieval of Neanderthal mitochondrial DNA, a work directed by Svante Pääbo and published in *Cell* in 1997. This was a turning point in the ancient DNA field and a landmark in the study of human evolution. I was in Oxford then and remember reading it with sheer excitement and dreaming that maybe one day, I would be also able to retrieve DNA from a Neanderthal. (It took me seven more years to reach this goal thanks to the discovery of Neanderthals at the El Sidrón site in Spain.) Somehow, it is sad that I won't be able to experience the excitement of retrieving the first Neanderthal DNA again. But at the same time, you can never watch a movie or read a book the same way you did for the first time. I guess it is a question of continuously looking for new, impossible challenges, and thus keeping one's enthusiasm alive.

What was it like to be a Neanderthal? It's very difficult to imagine what a different human species would be like, because we are the only surviving human species (note, however, that the concept of a single humankind is a very recent one). I think Neanderthals were essentially humans like us, even if they may have differed in some fundamental aspects, including probably several cognitive traits. If they were around today, we would without problems have included them in an expanded definition of humankind.

Why is El Sidrón, the site you study, such a special place for Neanderthals? El Sidrón makes you believe in paleontological miracles. All evidence indicates that there was a single Neanderthal family group

that was killed and cannibalized in a single event, some 49,000 years ago. This makes it a unique opportunity for investigating intragroup diversity, kinship structure, mating behaviour or reproductive patterns that are not going to be approachable anywhere else in the scattered fossil record.

You must collaborate a lot with archaeologists and paleontologists, what is that like? In the ancient DNA field, samples are scarce and sometimes unique, and thus having access to them is crucial for the success of a particular project. Therefore, we need to deal with archaeologists and paleontologists and also try to understand their specific goals and methodologies. They are both strange but interesting communities, influenced by schools of thought and dominated by strong characters — though I would say that the latter trait is certainly also present in the ancient DNA field. People in these areas are used to making inferences based on very little evidence; sometimes they hold their views even if they're clearly wrong and even try to prevent new research for purely academic and personal reasons. This is very surprising for a geneticist.

What is the best career advice you've been given? Many years ago, Jaume Bertranpetit (a professor of genetics here at my institute) told me: "don't stop doing things just because you don't have funding for them; money can always be found, but a timely good idea is priceless". Someone wanting to start a career in biology, I would advise

to be always curious, to keep reading papers from other fields even if they seem marginal to your own scientific interests, and to avoid trying to have everything perfectly planned; as Yogi Berra said, "Some things don't always work out the way you plan. The main thing is to keep trying, do better next time, and deal with disappointment if it comes."

What has been your biggest error? Back at the beginning of this century, I used to say "I am going to spend the rest of my life trapped in a mitochondrion!". This was because I was convinced that it was never going to be possible to retrieve even partial extinct genomes. Now, there are genomic sequences for many ancient humans and animals. This goes back to the famous Arthur C. Clarke quote: "When a distinguished, but elderly, scientist states that something is possible, he is almost certainly right. When he states that something is impossible, he is very probably wrong".

Do you have a favourite conference? I usually don't go to conferences. I think from an exclusively scientific point of view they are quite anachronistic. They were invented in the 19th century when the current technological means of global communication didn't exist, and some scientists could have spent decades working a particular subject in isolation. I agree they can be useful for social purposes, but I usually prefer to stay at home with my wife and children.

Speaking of technology, what do you think about the 'electronic revolution' in publishing? Science is experiencing the digital revolution, probably faster than other area of society. If you think of it this way, it is surprising that we are still publishing paper journals. Who on earth would be waiting for the latest issue of *Current Biology* to arrive at the university library to read it?

So, you think the conventional way of publishing is on its way out? The peer-review system is so odd that, if you try to explain how it works to someone outside the business, that person will surely have problems to understand it. According to Richard Horton, editor of *The Lancet*, "we know that the system of peer review is biased, unjust, unaccountable, incomplete, easily fixed, often insulting, usually ignorant, occasionally foolish, and frequently wrong." I have the feeling that the communication of scientific results will be totally different in the future. Maybe scientists will upload their research in some open webs where other scientists will discuss or criticize the findings online, ask for additional experiments, upload their own results, *etc*.

Do you have a scientific hero? In 20th century biology, William D. (Bill) Hamilton is probably the person who I admire the most. He published few papers, many in the *Journal of Theoretical Biology* — not precisely a high-impact journal, but they changed fundamental aspects of evolutionary biology. Intriguingly, he is almost entirely unknown outside the scientific community — if you mention Hamilton, most people will think of the Formula One driver.

You have written several popular science books. Would you consider this part of a scientist's duties? I think a scientist has somehow the obligation of communicating knowledge to society, specially in fields that may have profound social implications, such as human genetics and human evolution. I work trying to uncover fascinating things about extinct humans, but my research is not only about the past. In truth, it is also about us, about what makes us different. It is, of course, much easier to write books about your own research if you are very passionate about it.

What is your greatest ambition? I am planning to retrieve and study complete ancient genomes from European prehistory. Having published papers on sequences that were just 47 nucleotides long, this is a great conceptual leap for me! I am quite sure that in the future we will have hundreds of ancient genomes and we will be able to directly study evolution in time and place. However, we are accumulating a huge body of genomic data, but we are less able to interpret the functional impact of the genetic differences we find. We still need to better understand the relationship between genotype and phenotype. But, the next years are going to be great fun, I think.

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Quick guide

Catch bonds

Samuel Hertig and Viola Vogel

What are catch bonds? For a long time, the biophysics community searched for receptor–ligand bonds that could act like molecular hooks, dissociating easily in the absence of force but holding firm when stretched by tensile forces. While such hook-like bonds have not yet been found, a conceptually different type of force-activated bond was identified ten years ago that is now commonly referred to as a catch bond. These catch bonds are receptor–ligand bonds whose lifetime increases with tensile force applied to the bond (in contrast to the more prevalent slip bonds, whose lifetime is shortened by tensile forces acting on the bond).

What proteins are involved in catch bonds? To cope with tensile forces, we know today that a variety of bacterial and cellular adhesion molecules have evolved special mechanisms to strengthen their adhesive interactions. Cells and microbes often have to hold on to surfaces or to other cells while tensile forces put strain on their adhesion receptors. The tensile forces typically originate from dragging forces imposed by fluid flow acting on cells or bacteria, or from biological motors pulling on protein filaments or networks.

Since the discovery of the first catch bond, involving the bacterial adhesin FimH from *Escherichia coli*, various eukaryotic adhesins, including selectins and integrins, have also been found to form catch bonds with their respective ligands (Figure 1). The common feature of the few proteins identified so far to form catch bonds is that they all serve adhesive functions under conditions where cells or bacteria have to be able to adhere to surfaces, or to cells or tissues in the presence of tensile forces.

When do cells have to rely on catch bonds? Among the many adhesins that bacteria use to adhere to and later invade their hosts, *E. coli*